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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/940,682	08/27/2001	David E. Townsend	150026.464	4343

500 7590 08/09/2006

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EXAMINER	
FORD, ALLISON M	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 08/09/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/940,682	TOWNSEND, DAVID E.	
	Examiner	Art Unit	
	Allison M. Ford	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-7 and 10-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7 and 10-16* is/are rejected.

7)☒ Claim(s) 4 is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's response filed 2 June 2006 have been received and entered into the case. Claims 1 and 7 have been amended. Claims 8, 9 and 17-24 are cancelled. Claims 1-7 and 10-16 remain pending.

Priority

Acknowledgement is made of applicant's claim for priority to provisional application 60/228,956, filed 28 August 2000, priority under 119(e) is granted.

Applicant's claim for the benefit as a CIP of prior-filed application US 08/484,593 (now US Patent 6,387,650) under 35 U.S.C. 120 is also acknowledged.

However, applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 08/484,593, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Specifically, the current application claims a composition comprising a conditionally detectable marker and an aminopeptidase substrate, wherein the aminopeptidase substrate comprises a signal moiety that is detectable upon cleavage. Claim 7 requires the conditionally detectable marker to be tetrazolium red. While 08/484,593

discloses a composition that comprises an aminopeptidase substrate comprising a signal moiety, wherein the signal moiety can be cleaved to produce a detectable signal, it does not teach or suggest tetrazolium red as the species of signal moiety.

The only mention of tetrazolium in the application is in the background information, wherein applicants discuss the methods of the prior art, specifically Bochner US Patent 4,129,483, who uses tetrazolium (including tetrazolium red) to chemically detect the presence of target microbes, this patent is incorporated by reference. However, while Bochner discloses use of tetrazolium red as a conditionally detectable marker to detect target microbes, the parent application does not teach or suggest using tetrazolium red in their invention. The mere mention of tetrazolium (including tetrazolium red) in discussion of a prior art process does not render obvious use of tetrazolium red in the composition of the parent application. It is neither taught nor suggested anywhere in the parent application to use tetrazolium red in the composition; therefore, it remains that parent application 08/484,593 does not provide support for a composition comprising tetrazolium red as part of the claimed composition.

Thus the subject matter of claim 7 is not disclosed in the parent application; however, the subject matter of claim 7 is disclosed in provisional application 60/228,956, and as such, the effective filing date of the subject matter of claim 7 is determined to be 28 August 2000. The effective filing date of the subject matter of claims 1-6 and 10-16 is determined to be 7 June 1995.

Claim Objections

Claim 4 is objected to because in the species *E. coli* OH157, the strain identifier "OH157" should not be italicized. Correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6 and 10-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

"An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention... one must define a compound by 'whatever characteristics sufficiently distinguish it'. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process." MPEP § 2163

Applicant claims a composition for detecting a target microorganism, the composition comprising (i) a conditionally detectable marker; and (ii) a substrate for an aminopeptidase, wherein said aminopeptidase is substantially absent from the target microorganism, and wherein said substrate comprises a signal moiety that provides a detectable signal when cleaved by substantially all non-target microorganisms.

Regarding the 'conditionally detectable marker' applicant has failed to describe a sufficient description of a representative number of species which is required to claim the entire genuses of 'conditionally detectable markers'. The claim is drawn to a genus of molecules, the genus being all 'conditionally detectable markers', it has been held that in order to satisfy the written description requirement for a claimed genus a representative number of species from the

genus by disclosure of relevant, identifying characteristics, such as structure or other physical or chemical properties, or functional characteristics; furthermore, in the instant case, where the genus is extremely varied, it has been held that when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. It is noted that the specification teaches the 'conditionally detectable marker' to be a molecule that undergoes a measurable change, such as a color change, when reacted upon by a viable microorganism in a sample; disclosed species include Vital Dyes, particularly red-ox dyes resazurin, XTT, MTT, and tetrazolium red (Spec, paragraph spanning pages 8-9).

However, while applicant has disclosed several species of red-ox dyes that can be used as 'conditionally detectable markers' this is not considered sufficient to represent the entire varied genus of 'conditionally detectable markers'. One of ordinary skill in the art will recognize that the genus 'conditionally detectable markers' includes any molecule, protein, chemical, or object that alters its behavior under some conditions, and not under others, can be considered a 'conditionally detectable marker'. Applicants have failed to even limit the genus by limiting the *conditions* during which the marker can be detected. Therefore, within the genus, as claimed, one can interpret 'conditionally detectable markers' to include *any* chemical, molecule, protein, object, etc, that changes *any* physical or chemical property in response to *any* change in environment. Thus the genus of conditionally detectable markers can include genes that are induced to express under certain conditions (i.e. β-gal-lactose); proteins that fluoresce under specific conditions (i.e. luciferase); polymers that change state of matter under certain conditions (i.e. hyaluronic acid); or even objects that physically change under specific conditions (i.e. light bulb illuminating upon flow of current through filament). Clearly, applicants' disclosure of markers detectable by color change, specifically red-ox dyes, does not represent the extremely broad genus of 'conditionally detectable markers' and thus applicants have failed to satisfy the written description requirement.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-7 and 10-16 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Applicant claims a composition for detecting a target microorganism, the composition comprising (i) a conditionally detectable marker; and (ii) a substrate for an aminopeptidase, wherein said aminopeptidase is substantially absent from the target microorganism, and wherein said substrate comprises a signal moiety that provides a detectable signal when cleaved by substantially all non-target microorganisms. The target microorganism is a bacteria, yeast, mold, fungi, protozoa or virus, specifically bacteria selected from Salmonella, Listeria, E.coli OH157, Campylobacter, Staphylococcus aereus, Cryptosporidium or Giardia. The preferred bacteria are Campylobacter. The conditionally detectable marker is detectable by a color change, wherein the change in color is produced by a biochemical reduction of tetrazolium red. The enzyme is specifically L-alanine aminopeptidase; and the substrate is selected from a disclosed group, specifically L-alanin-7-amido-4-methylcoumarin. The non-target microorganisms are substantially all non-Campylobacter species. The composition further comprises a growth supporting medium for target microorganisms, which contains all necessary nutrients and growth conditions to support target organisms.

Claim 1 remains unclear. As amended the claim now requires the composition to comprise two components: (i) a conditionally detectable marker; and (ii) an aminopeptidase substrate which comprises a signal moiety that is capable of providing a detectable signal when cleaved. Regarding the conditionally detectable marker, the claim fails to particularly point out

or describe the conditions in which the marker is detectable. It is noted that in applicant's response they have described the conditionally detectable marker as a 'presumptive positive' marker which reacts with both viable target microorganisms and any viable non-target microorganisms to produce a measurable signal; however, the claim does not state this functional limitation (reaction with both target and non-target microorganisms) or any other structural limitation (such as the conditions in which the marker can be detected or specific formula of the marker). Therefore it appears the claim is omitting essential elements from the claim, the essential elements being the conditions in which the conditionally detectable marker is detectable

Applicant's claim 13 stands rejected as being dependent upon a cancelled base claim (8); therefore the scope of claim 13 cannot be envisioned.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6 and 10-16 stand rejected under 35 U.S.C. 102(b) as being anticipated by Carr et al (US Patent 5,064,756).

Applicant claim 1 is directed to a composition for detecting a target microorganism, the composition comprising (i) a conditionally detectable marker; and (ii) a substrate for an aminopeptidase, wherein said aminopeptidase is substantially absent from the target microorganism, and wherein said substrate comprises a signal moiety that provides a detectable signal when cleaved by substantially all non-target microorganisms. Claim 6 requires the conditionally detectable marker to be detectable by a color change. Claim 10 requires the enzyme

to specifically be L-alanine aminopeptidase. Claims 11 and 12 require the substrate to be selected from the disclosed group, specifically L-alanin-7-amido-4-methylcoumarin. Claims 14 and 15 require the composition to further comprise a growth supporting medium for target microorganisms, which contains all necessary nutrients and growth conditions to support target organisms. Claim 16 requires the composition of 14 to further comprise antibiotics. Claims 2-5 and 13 are directed to the intended use of the composition (detection of specific microorganisms), these claims recite specific target microorganisms as well as the non-target microorganisms the composition is to detect.

With regards to claims 2-5 and 13, which are related to the intended use of the composition (detection of specific microorganisms), please note that in cases where the body of the claim fully and intrinsically sets forth all the limitations of the invention, such as all components of a composition, recitations that merely states the intended use of the composition, rather than any distinct definition of any of the claimed invention's limitations, are not considered limitations and are of no significance to claim construction. See MPEP § 2111.02. Therefore, claims 2-5 and 13 are given no patentable weight and have been included in the rejection of the claims directed to the composition.

Carr et al teaches a kit for antibiotic sensitivity testing, comprising a prepared microtitre plate which contains active materials for promoting growth of the microbe sample (which applicant calls a growth supporting medium which comprises all necessary nutrients and growth conditions to properly support growth of microorganisms), antibiotics, and one or more fluorogens (See Carr et al, col. 5, ln 7-24 & col. 6, ln 4-16). As the fluorogen, Carr et al uses the hydrolysable derivatives of 4-methylcoumarin, particularly 7-N-(alanyl)-7-amido-4-methylcoumarin, which produce a detectable change in color upon cleavage by an aminopeptidase (See Carr et al, col. 4, ln 36-50, col. 6, ln 17-26 & claims). Therefore, in their kit for antibiotic sensitivity testing, Carr et al includes microtitre plates comprising growth substrate

containing appropriate nutrients and materials for supporting growth of the non-target microorganisms (non-contaminating microbes), antibiotics, and the fluorogenic L-alanine-aminopeptidase substrate 7-N-(alanyl)-7-amido-4-methylcoumarin, which is also considered a 'conditionally detectable marker' (Claims 1-6 and 10-16); therefore the reference anticipates the claimed subject matter.

Claims 1-6 and 10-13 stand rejected under 35 U.S.C. 102(b) as being anticipated by Manafi et al (J. Applied Bacteriology, 1990).

Applicant claim 1 is directed to a composition for detecting a target microorganism, the composition comprising (i) a conditionally detectable marker; and (ii) a substrate for an aminopeptidase, wherein said aminopeptidase is substantially absent from the target microorganism, and wherein said substrate comprises a signal moiety that provides a detectable signal when cleaved by substantially all non-target microorganisms. Claim 6 requires the conditionally detectable marker to be detectable by a color change. Claim 10 requires the enzyme to specifically be L-alanine aminopeptidase. Claims 11 and 12 require the substrate to be selected from the disclosed group, specifically L-alanin-7-amido-4-methylcoumarin. Claims 2-5 and 13 are directed to the intended use of the composition (detection of specific microorganisms), these claims recite specific target microorganisms as well as the non-target microorganisms the composition is to detect.

With regards to claims 2-5 and 13, which are related to the intended use of the composition (detection of specific microorganisms), please note that in cases where the body of the claim fully and intrinsically sets forth all the limitations of the invention, such as all components of a composition, recitations that merely states the intended use of the composition, rather than any distinct definition of any of the claimed invention's limitations, are not considered limitations and are of no significance to claim construction. See MPEP § 2111.02. Therefore,

claims 2-5 and 13 are given no patentable weight and have been included in the rejection of the claims directed to the composition.

Manafi et al teach a composition comprising the conditionally detectable marker L-alanine-7-amido-4-methylcoumarin (AAMC), which produces a fluorescent color change when cleaved by the L-alanine-aminopeptidase found in the cell wall of Gram-negative bacteria (See Manafi et al, See pages 823-827). The AAMC is both a conditionally detectable marker and an aminopeptidase substrate (Claims 1-6 and 10-13). Therefore the reference anticipates the claimed subject matter.

Claims 1-7 and 13 stand rejected under 35 U.S.C. 102(e) as being anticipated by Tuompo et al (US Patent 5,420,017).

Applicant claim 1 is directed to a composition for detecting a target microorganism, the composition comprising (i) a conditionally detectable marker; and (ii) a substrate for an aminopeptidase, wherein said aminopeptidase is substantially absent from the target microorganism, and wherein said substrate comprises a signal moiety that provides a detectable signal when cleaved by substantially all non-target microorganisms. Claim 6 requires the conditionally detectable marker to be detectable by a color change. Claim 7 requires the conditionally detectable marker to be tetrazolium red. Claims 2-5 and 13 are directed to the intended use of the composition (detection of specific microorganisms), these claims recite specific target microorganisms as well as the non-target microorganisms the composition is to detect.

With regards to claims 2-5 and 13, which are related to the intended use of the composition (detection of specific microorganisms), please note that in cases where the body of the claim fully and intrinsically sets forth all the limitations of the invention, such as all components of a composition, recitations that merely states the intended use of the composition,

rather than any distinct definition of any of the claimed invention's limitations, are not considered limitations and are of no significance to claim construction. See MPEP § 2111.02. Therefore, claims 2-5 and 13 are given no patentable weight and have been included in the rejection of the claims directed to the composition.

Tuompo et al teach a composition for detecting the presence of Gram-negative bacteria, wherein the composition comprises a test solution comprising a chromogenic reagent in an amount effective to detect the Gram negative bacteria; preferably the chromogenic reagent is a tetrazolium salt, particularly triphenyltetrazolium chloride (tetrazolium red), which produces a color change from colorless to red upon biochemical reduction (which applicant calls a conditionally detectable marker comprising a signal moiety). Therefore the reference anticipates the claimed subject matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6 and 10-13 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Carr et al (US Patent 5,064,756).

Applicant claim 1 is directed to a composition for detecting a target microorganism, the composition comprising (i) a conditionally detectable marker; and (ii) a substrate for an aminopeptidase, wherein said aminopeptidase is substantially absent from the target microorganism, and wherein said substrate comprises a signal moiety that provides a detectable signal when cleaved by substantially all non-target microorganisms. Claim 6 requires the

conditionally detectable marker to be detectable by a color change. Claim 10 requires the enzyme to specifically be L-alanine aminopeptidase. Claims 11 and 12 require the substrate to be selected from the disclosed group, specifically L-alanin-7-amido-4-methylcoumarin. Claims 14 and 15 require the composition to further comprise a growth supporting medium for target microorganisms, which contains all necessary nutrients and growth conditions to support target organisms. Claim 16 requires the composition of 14 to further comprise antibiotics. Claims 2-5 and 13 are directed to the intended use of the composition (detection of specific microorganisms), these claims recite specific target microorganisms as well as the non-target microorganisms the composition is to detect; however claims 2-5 and 13 are given no patentable weight and have been included in the rejection of the claims directed to the composition, see above.

Carr et al teaches a kit for antibiotic sensitivity testing, comprising a prepared microtitre plate which contains active materials for promoting growth of the microbe sample (which applicant calls a growth supporting medium which comprises all necessary nutrients and growth conditions to properly support growth of microorganisms), antibiotics, and one or more fluorogens (See Carr et al, col. 5, ln 7-24 & col. 6, ln 4-16). As the fluorogen, Carr et al uses the hydrolysable derivatives of 4-methylcoumarin, particularly 7-N-(alanyl)-7-amido-4-methylcoumarin, which produce a detectable change in color upon cleavage by an aminopeptidase, which is also considered a 'conditionally detectable marker' (See Carr et al, col. 4, ln 36-50, col. 6, ln 17-26 & claims).

While Carr et al does teach that derivatives of 4-methylcoumarin can be used in their invention, they do not teach the specific amino acid-containing derivatives that are presently claimed. However, it would have been well within the purview of one of ordinary skill in the art, at the time the invention was made, to use any of the well known amino acid-containing derivatives of 4-methyl-coumarin, including L-alanine-7-amido-4-methylcoumarin TFA, L-alanine-7-amido-4-trifluoro-methylcoumarin TFA, L-alanyl-L-alanyl-L-phenylalanine-7-amido-

4-methylcoumarin, and L-alanyl-L-alanyl-L-phenylalanine-7-amido-4-methylcoumarin TFA. One would have been motivated to use any of the well known derivatives and would have expected success because the prior art teaches the detectable change in fluorescence is due to the cleavage of the peptide bond, which releases the methylcoumarin fluorogen; attachment of any amino acid residue to the amido methylcoumarin would present the appropriate bond for cleavage. Furthermore, Carr et al exemplify -N-(alanyl)-7-amido-4-methylcoumarin as the substrate, which is cleaved by an L-alanine aminopeptidase; therefore, one of ordinary skill in the art would have been motivated to use other L-alanine aminopeptidase substrates, such as those listed above, as they are functional equivalents for testing the presence of L-alanine aminopeptidase. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Claims 1-6 and 10-13 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Manafi et al (J Applied Bacteriology, 1990).

Applicant claim 1 is directed to a composition for detecting a target microorganism, the composition comprising a conditionally detectable marker that is a substrate for an aminopeptidase; wherein the substrate comprises a signal moiety linked to the substrate that provides a detectable signal when cleaved. Claim 6 requires the conditionally detectable marker to be detectable by a color change. Claim 10 requires the enzyme to specifically be L-alanine aminopeptidase. Claims 11 and 12 require the substrate to be selected from the disclosed group, specifically L-alanin-7-amido-4-methylcoumarin. Claims 14 and 15 require the composition to further comprise a growth supporting medium for target microorganisms, which contains all necessary nutrients and growth conditions to support target organisms. Claim 16 requires the composition of 14 to further comprise antibiotics. Claims 2-5 and 13 are directed to the intended use of the composition (detection of specific microorganisms), these claims recite specific target

microorganisms as well as the non-target microorganisms the composition is to detect; however claims 2-5 and 13 are given no patentable weight and have been included in the rejection of the claims directed to the composition, see above.

Manafi et al teach a composition comprising the conditionally detectable marker L-alanine-7-amido-4-methylcoumarin.(AAMC), which produces a fluorescent color change when cleaved by the L-alanine-aminopeptidase found in the cell wall of Gram-negative bacteria (See Manafi et al, See pages 823-827).

Manafi et al exemplify L-alanine-7-amido-4-methylcoumarin as the substrate, which is cleaved by an L-alanine aminopeptidase; therefore, while they do not teach other derivatives of L-alanine-7-amido-methylcoumarin, it would be within the purview of one of ordinary skill in the art to select other functionally equivalent substrates, including L-alanine-7-amido-4-methylcoumarin TFA, L-alanine-7-amido-4-trifluoro-methylcoumarin TFA, L-alanyl-L-alanyl-L-phenylalanine-7-amido-4-methylcoumarin, and L-alanyl-L-alanyl-L-phenylalanine-7-amido-4-methylcoumarin TFA. It is known that the L-alanine aminopeptidase will cleave the substrate at the L-alanine residue to release the amido-methylcoumarin fluorogen, substitution of different substrates that comprise the same L-alanine-7-amido-4-methylcoumarin core would be expected to function equivalently, especially in absence of evidence to the contrary. Therefore, one of ordinary skill in the art would be motivated to use the derivatives of L-alanine-7-amido-4-methylcoumarin listed above as alternatives to the substrate of Manafi et al, and would expect success in doing so, based on the fact that the functional core structure remains unchanged, and thus the derivatives would be considered functional equivalents. Therefore the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Response to Arguments

Applicant's arguments filed 2 June 2006 have been fully considered, but are not found persuasive.

Applicants feel the Office Action has misinterpreted their invention, applicants characterize their invention as a composition comprising two separate markers, the first being the 'conditionally detectable marker' (exemplified as tetrazolium red) which produces a detectable signal upon contact with either viable target microorganisms or viable non-target microorganisms, the second marker being the 'aminopeptidase substrate comprising a signal moiety' (exemplified as the methylcoumarin substrates listed in claim 11, especially L-alanine-7-amido-4-methylcoumarin) which produces a detectable signal only upon cleavage by an appropriate aminopeptidase which is only found in non-target microorganisms. Applicants submit the composition indicates the presence of *target* microorganisms when the first marker (the 'conditionally detectable marker') produces a signal, but the second marker (the signal produced by the cleavage of the aminopeptidase substrate) does not produce a signal. Applicants argue that their composition is patentable over the compositions of the prior art because none of the prior art compositions disclose or suggest the combination of detectable markers to detect microorganisms.

Initially, an error is noted in applicants analysis system described above: if a test sample comprising both target and non-target microorganisms is applied to the composition of claim 1, then both the first and the second markers would produce a detectable signal, which according to applicants interpretation above, would *not* indicate the presence of the target microorganism, but such would be a false reading. Following applicants' analysis method outlined in the Response, the composition of claim 1 would only be effective to detect target microorganisms in samples *substantially free of non-target microorganism*, it would not be effective to merely *detect a target microorganism*, as claimed.

However, despite the problems with analysis of the testing system, the claims at hand are drawn not to a method of testing, but to a composition *per se*, said composition comprising (i) a conditionally detectable marker; and (ii) an aminopeptidase substrate comprising a signal moiety which provides a detectable signal upon cleavage. It is noted that the claims do not require components (i) and (ii) to be separate components, thus a single component which can satisfy both functional and structural limitations reads on the instant invention. Also, it is noted that applicants attempt to define the aminopeptidase substrate by stating the aminopeptidase is substantially absent from the target microorganism; however, this limitation is not given patentable weight because applicants only limit the aminopeptidase by stating it is substantially absent from target microorganisms. It is improper to define one element (the aminopeptidase) in reference to another element that is variable (the target microorganism). In the instant case the target microorganism is not defined, but rather can vary based on the application; therefore, one of ordinary skill in the art cannot immediately envisage which aminopeptidases are and are not present in 'the target microorganism' because 'the target microorganism' can be different each time. This is particularly problematic because the distinction between 'target' and 'non-target' microorganisms is subjective and variable, for 'target' microorganisms are defined in the specification as "any viable unicellular microorganism the detection of which is required to determine the quality, safety or other specification of a particular test sample" (Spec Pg. 11, ln 4-6); thus the target microorganism may be changed depending on the specifications of the test. Therefore, the limitation that the aminopeptidase is substantially absent from the target microorganism is not given patentable weight.

Applicants' arguments are considered in view of the above. In response to the art rejections applicants argue that none of the cited references teach or suggest a composition comprising a conditionally detectable marker in addition to a substrate for an aminopeptidase; however, as discussed above, it is noted that the claims do not require the two components to be separate. Therefore, a single component which functions as both a 'conditionally detectable marker' and a substrate for an aminopeptidase, such as the hydrolysable derivatives of 4-methylcoumarin, particularly 7-N-(alanyl)-7-amido-4-methylcoumarin of Carr et al, the L-alanine-7-amido-4-methylcoumarin (AAMC) of Manafi et al, and/or the triphenyltetrazolium chloride of Tuompo et al, read on the instant invention.

Applicants further argue that the compositions of the cited references Carr et al, Manafi et al and/or Tuompo et al do not teach a composition comprising a substrate for an aminopeptidase, wherein the aminopeptidase is substantially absent from the target microorganism, rather the aminopeptidase substrates in the compositions of Carr et al, Manafi et al and Tuompo et al are hydrolysable by aminopeptidases found in the *target* microorganisms, not in the *non-target* microorganisms. This is not found persuasive because, again, the term *target* and *non-target* microorganisms are subjective; the terms *target* and *non-target* are assigned based on individual tests, the labels could simply be switched to read upon the instant invention. As discussed above, because applicants define "the aminopeptidase" only in reference to the "target microorganisms" (which is a variable) this limitation is not given patentable weight, and thus these arguments are not persuasive.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Allison M. Ford whose telephone number is 571-272-2936. The examiner can normally be reached on 7:30-5 M-Th, alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Allison M Ford
Examiner
Art Unit 1651

LEON B. LANKFORD, JR.
PRIMARY EXAMINER